**Vaccines and Related Biological Products Advisory Committee Meeting**
**June 16, 2023**
**Strain selection for updated COVID-19 vaccines for the 2023-2024**

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**Capsule**
These comments are submitted in advance of VRBPAC's meeting to consider updated Covid-19 pro-vaccines for the 2023-24 season. At the time of writing to meet the deadline of submission of comments for consideration by VRBPAC members (June 7), FDA have not yet disclosed their briefing materials that would allow more focused comments to be made.

Accordingly, the purpose of this document is to make general comments applicable to the VRBPAC meeting based on a framework that is likely to be based on the WHO statement, as well as ongoing, unresolved issues.

The pandemic is over. Cases, hospitalizations, and deaths have declined despite only 17% of those eligible having received the bivalent booster. (CDC Data Tracker June 7 2023). Although certain EUA provisions have been extended, with the many outstanding concerns reviewed below, why does FDA appear to maintain this strategy when it was being questioned by both FDA's Dr. Marks and NIH's Dr. Fauci as soon as about three months after the deployment of the updated BA.4/5 boosters?

We append our extensive comments on FDA's briefing document for the January 26 2023 VRBPAC meeting which add to the challenges to the Covid-19 vaccination strategy.

We also append our comments submitted recently to the National Academies on March 30 2023 that summarizes our extensive work and comments to FDA and CDC since 2021 on the topic of vaccine safety and gene therapy.

Given the low benefit of the Covid-19 vaccines currently, and their likely waned, evaded or negative effect by the time of deployment, as well as the significant safety concerns, the risks of using these products outweighs the benefits and a new strategy must be implemented.

Attachments
Wiseman2023-VRBPACJan23-FDA-2022-N-2810-CommentsonBrefingDocument-TRACKING.pdf
Wiseman-NAS-Mar30-CovidVaccineAdverseEvents.pdf

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## 1. Preface
At the outset we point out our use of the term "pro-vaccine" since the modRNA products do not contain the target antigens as in a conventional vaccine. Rather they contain the genetic instructions that are read by a patient's body to produce the target spike protein antigen by translation. Because this is somewhat analogous to the conversion of a pro-drug to an active form,(1) we employ the term "pro-vaccine."

## 2. Introduction
FDA has convened a meeting of its VRBPAC for June 15th 2023. The stated purpose[1] is:

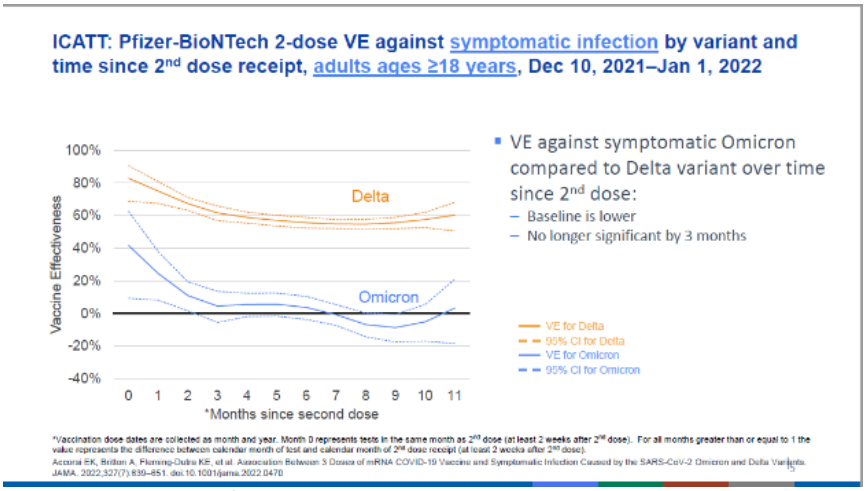
[1] www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-june-15-2023-meeting-announcement#event-materials

*"to discuss and make recommendations on the selection of strain(s) to be included in the periodic updated COVID-19 vaccines for the 2023-2024 vaccination campaign. This discussion will include consideration of the vaccine composition for fall to winter, 2023-2024."*

The meeting is the latest of a series convened by FDA or CDC to discuss changes in the strain of the target antigen in Covid-19 pro-vaccines. We have submitted comments to these meetings as indicated in this table.

| Date | Year | Agency | Committee | Ref |
|---|---|---|---|---|
| 4/6 | 2022 | FDA | VRBPAC | (2) |
| 4/20 | 2022 | CDC | ACIP | (3) |
| 9/1 | 2022 | CDC | ACIP | (4) |
| 10/19 | 2022 | CDC | ACIP | (5) |
| 1/26 | 2023 | FDA | VRBPAC | (6) |
| 2/24 | 2023 | CDC | ACIP | (7) |
| 4/19 | 2023 | CDC | ACIP | (8) |

These meetings were held based on the public acknowledgement by regulators that the efficacy of the Covid-19 vaccines and their boosters could wane with significant escape by the Omicron strain and its subvariants. As we noted as early as January 2022 (9) VE against Omicron could even become negative. Although not specifically acknowledged by FDA or CDC, data were released similar to those depicted in the graph below presented by CDC's Dr. Link-Gelles at the VRBPAC meeting of June 14 2022 showing negative VE by about 7 months, following zero VE at about 3 months post-vaccination.



Dr. R. Link-Gelles, VRBPAC, June 14 2022 [2]

Against this background, in June 2022 VRBPAC voted to recommend that bivalent (Wuhan + BA.4/5) Covid modRNA vaccines be developed for a Fall 2022 surge anticipated by modelling. FDA did indeed issue EUAs for Pfizer and Moderna bivalent vaccines based on eroded scientific standards and a paucity of data based on an extrapolative approach, as we have commented.(4,5)

In April 2023, in an effort to simplify the confusing array of formulations and doses available for the modRNA pro-vaccines, FDA withdrew the EUAs for the monovalent versions, with the bivalent versions to be used as primary doses. Recognition was given to the contribution of naturally acquired immunity. Although no VRBPAC meeting was convened on this subject, CDC's ACIP did meet, for which we provided comments.(8)

In all of these meetings, FDA expressed the view that strain updates would be necessary as the SARS-Cov-2 continued to mutate and evade vaccine immunity, in a manner somewhat analogous to the yearly revision of flu vaccine composition. FDA did recognize important differences between the influenza and coronaviruses, notably in the lack of established seasonality and rapid mutation rate for the latter. Nonetheless, to optimize public acceptance of updated pro-vaccines and t avoid "vaccine fatigue," it was felt that a once-yearly revision would be the most practical. Since respiratory infections, mainly driven by the flu, occurred in the Fall and Winter, it was felt that updated Covid-19 pro-vaccines should be deployable

[2] fda.gov/media/159225/download

in the Fall. A decision would need to be made as to the most appropriate target strain(s) as close to the Fall as possible, in the hope that any mutations occurring after that would be sufficiently immunologically similar to the new strain to provide some level of protection.

Based on the logistics of manufacturing, the latest time that such a decision could be made every year is June, hence the VRBPAC meeting on June 15th.

Any decision by US public health officials (FDA, CDC) is not made entirely in isolation and the views of other bodies are considered, although not controlling. On May 18 2023 the WHO recently issued a *"Statement on the antigen composition of COVID-19 vaccines"*(10) based on the work of their WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC). At that time the globally predominant XBB.1 descendent lineages (XBB.1.5, XBB.1.16, and XBB.1.9) were found to be, based on neutralizing antibody titres, highly evasive to the original monovalent or BA.1 or BA.4/5 -containing bivalent pro-vaccines. The WHO statement contained the following main points:

- Individuals with hybrid immunity due to any SARS-CoV-2 infection show higher neutralizing antibody titers against XBB.1 descendent lineages as compared to responses from vaccinated individuals who had no evidence of infection.
- New formulations of COVID-19 vaccines be directed at XBB descendent lineages, such as monovalent XBB.1.5 or XBB 1.16.
    - Preclinical data shared by vaccine manufacturers show that XBB.1 descendent lineage-containing candidate vaccines elicit higher neutralizing antibody responses to currently circulating SARS-CoV-2 variants, compared to responses elicited by currently approved vaccines.
- The inclusion of the index virus in a multivalent pro-vaccine is advised against because:
    - The index virus no longer circulates and its antigen elicits very low levels of neutralizing antibodies against currently circulating variants
    - There is *in vitro* evidence that immune imprinting [original antigenic sin]
    - Its inclusion reduces the concentration of the new target antigen(s) as compared to monovalent vaccines, which may decrease the magnitude of the humoral immune response [this statement does not consider the unknown relationship between modRNA dose and amount of spike protein translated by patients]

At the time of writing to meet the deadline of submission of comments for consideration by VRBPAC members (June 7), FDA have not yet disclosed their briefing materials that would allow more focused comments to be made.

Accordingly, the purpose of this document is to make general comments applicable to the VRBPAC meeting based on a framework that is likely to be based on the WHO statement, as well as ongoing, unresolved issues.

Acknowledgements: I am grateful to a number of colleagues with whom I have collaborated and whose work is cited herein and referenced as "we."

## 3. Chasing Variants, Vaccination Strategy, Time for a Different Approach

The pandemic is over. Cases, hospitalizations, and deaths have declined despite only 17% of those eligible having received the bivalent booster. (CDC Data Tracker June 7 2023). Although certain EUA provisions have been extended, with the many outstanding concerns reviewed below, why does FDA appear to maintain this strategy when it was being questioned by both FDA's Dr. Marks and NIH's Dr. Fauci as soon as about three months after the deployment of the updated BA.4/5 boosters?

### 3.1. Drs. Marks and Fauci Question the Strategy about three months after Omicron boosters deployed

FDA's Dr. Peter Marks challenges this strategy. Writing in JAMA, December 9 2022 (11) he stated: *"Continuing along the current path of the generation and administration of variant-specific vaccine boosters is inadequate as a long-term strategy for addressing COVID-19 in populations globally."*

VRBPAC member Dr. Paul Offit appears to concur: *"The experience of the past year has taught us that chasing these Omicron variants with a bivalent vaccine is a losing game"* (cited in Time Magazine Jan 11 2023).[3]

Dr. Anthony Fauci authored a paper published January 11 2023 (12) with the following startling revelations:

[3] https://time.com/6246525/bivalent-booster-not-very-effective-paul-offit/

*"Viruses that replicate in the human respiratory mucosa without infecting systemically, including influenza A, **SARS-CoV-2**, endemic coronaviruses, RSV, and many other ''common cold'' viruses, cause significant mortality and morbidity and are important public health concerns. Because these viruses generally do not elicit complete and durable protective immunity by themselves, **they have not to date been effectively controlled by licensed or experimental vaccines**.*

*[…] if natural mucosal respiratory virus infections do not elicit complete and long-term protective immunity against reinfection, **how can we expect vaccines, especially systemically administered non-replicating vaccines, to do so?***

*[…] i**t is not surprising that none of the predominantly mucosal respiratory viruses have ever been effectively controlled by vaccines.***

*As of 2022, after more than 60 years of experience with influenza vaccines, very little improvement in vaccine prevention of infection has been noted. As pointed out decades ago, and still true today, **the rates of effectiveness of our best approved influenza vaccines would be inadequate for licensure for most other vaccine-preventable diseases"***

### 3.2. Our unposted challenge to the strategy at tehe January 26 VRBPAC Meeting.

If it was evident to Drs. Fauci and Marks, the wisdom of the strategy was also evident to us. We submitted comments to the VRBPAC Meeting of January 26th 2023 in the form of a detailed annotation to FDA's briefing document release prior to the meeting to discuss future strain composition for Covid-19 vaccines, simplification of the different formulations and dose schedules, and plans for future COVID-19 vaccine composition recommendations.

We received a confirmation of submission with tracking number ldc-mhyo-7aj3, but to this day, the comments have not been posted on the regulaitons.gov site, despite an email confirmation and assurance shown below.

From: CBER VRBPAC <CBERVRBPAC@fda.hhs.gov>
To: synechion@aol.com <synechion@aol.com>; <XXXX@fda.hhs.gov>
Cc: <XXXX@fda.hhs.gov>
Sent: Mon, May 15, 2023 2:25 pm
Subject: FW: [EXTERNAL] Re: Missing Comment Submitted on Regulations.gov (ID: FDA-2022-N-2810-0001)
Good afternoon, Dr. Wiseman
Thank you for your inquiry regarding the docket comment that you submitted. I have looked into it and reached out to my contact. He has answered back stating:
"comment was received as FDA-2022-N-2810-DRAFT-21456, its attachment is attached. I'm not sure what caused the delay for it be posted, but I believe since this docket is among those receiving the most comments in 2023 (21,606) and we asked for them to be posted on the back end, perhaps there was an issue. I'll try to get these posted in the near future".
Please feel free to contact me if you have any additional comments/concerns
Thanks VRBPAC Team

We have posted these elsewhere (6) and repost them attached to this current submission.

In summary we noted that:
*"FDA's justification for the use of current Wuhan/BA.5 bivalent vaccines as primary doses, comes from weak data. Most studies were performed before or during the era of the BA.5 strain, which is almost extinct. A number of studies cited by FDA point out the reduced antibody response to the now predominant BQ and XBB variants. Several important studies are missing from the discussion that highlight how futile the use of the current bivalent variant is likely to be.*

*This the current bivalent Covid-19 vaccines are obsolete.*

*FDA policy remains focused on the spike protein, known to be toxic. No discussion of alternate targets is provided and no acknowledgement that the bivalent vaccines may give rise to at least four heterotrimers, at least two of which represent novel pharmacology and likely toxicology.*

*FDA makes no note of the continued absence of an immune correlate of protection and continues to rely on neutralizing antibody studies. FDA appears to intend to not require extensive safety and efficacy testing for new variant vaccine versions.*

*There is no discussion of safety, or safety signals, as we have provided in various submissions to FDA (2,13-17) or CDC.(3,9,16-21). There is no discussion of the concerning safety signals evident in the recent FOIA disclosure of PRR signals from CDC.*

*These vaccines remain experimental. There is no discussion of the consequences of repeated dosing of these genetic vaccines, nor is there discussion related to the long-term consequences of these genetic vaccines and the failure of FDA to publicly involve the sections within FDA responsible for gene therapies. Long overdue studies on cancer, genotoxicity, sub-clinical myocarditis are not discussed.*

*Comparisons with policies regarding influenza vaccination should be made carefully, to avoid the impression that the Covid-19 genetic vaccines are similar in mechanism of action to classical vaccines such as those used for influenza."*

## 4. Continuing Concerns as to Pro-Vaccine Safety

We have provided extensive comments on this topic to FDA and CDC meetings. We have summarized this work in comments submitted recently to a committee of the National Academies convened on March 30 2023 to *"review relevant literature regarding adverse events associated with* [Covid-19] *vaccines."* (22) and provided as an attachment to this current submission.

In summary:
These comments contain a number of novel analyses conducted relating to Covid-19 vaccine safety. This document further discusses:

- Hasty vaccine development, undisclosed sequences and kinetics of modRNA and spike protein
- Novel heterotrimers formed after bivalent vaccination
- Gene therapy nature of the Pfizer, Moderna and Janssen Covid-19 vaccines
- VAERS underreporting
- Safety signal analysis
- Masking of safety signals
- Ischemic stroke
- Negative efficacy: an indicator of immune suppression?
- All-cause mortality and vaccination
- Concerning cancer reports
- Transparency, scientific engagement, rebuilding trust in public health

We show here a number of instances of FDA or CDC analyses being unreliable or highly limited.

According to a recent article in Nature,(23) Covid-19 vaccine hesitancy has spilled over to other vaccinations reaching their lowest point since 2008 and jeopardizing the health of millions. This is attributed an erosion of trust and confidence in governments and public-health institutions exacerbated with the advent of COVID-19 vaccines.

Restoring trust in public health institutions must surely be your highest priority. Unless the setting of parameters that will determine whether someone is eligible for compensation for alleged vaccine-injury is seen as just, there will be further erosion in trust of public health institutions, exacerbated as the specter of unknown long-term harms related to the hastily deployed novel gene therapy, becomes appreciated.

Restoration in trust can only be begin if your work is transparent and open to scientific dialog. Yours cannot be another exercise in "going through the motions" of the kind we have seen with FDA and CDC committees. My colleagues and I are ready to participate in meaningful and necessary scientific discourse.

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